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Exercise-based correlates to calcaneal osteogenesis produced by a chronic training intervention

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ABSTRACT

Thirty workouts on a gravity-independent device (Impulse Training Systems, Newnan GA) evoked significant calcaneal bone mineral content (BMC, +29%) and density (BMD, +33%) gains. High speeds and impact loads were produced per repetition. We examined exercise performance variables from the 30-workout intervention to identify correlates to delta (Δ) calcaneal BMC and BMD variance. Workouts included hip extension and seated calf press exercises done with subject's left legs. Δ values were obtained from the first and 12th workouts for the hip extension movement, and for the first and 24th workouts for the seated calf press exercise. Per exercise the following variables were quantified: peak force (ΔPF), peak acceleration (ΔPA), impulse (ΔI), and dwell times (ΔDT). Dwell times are the elapsed time between the end of the eccentric phase, and the start of the next repetition's concentric phase. Pearson Coefficients assessed correlations between performance and criterion variables. With hip extension ΔDT calculated with data from the first and 12th workouts, there were significant correlations with calcaneal ΔBMC ($r = -0.64$) and ΔBMD ($r = -0.63$). With seated calf press ΔDT derived as the difference from the first and 24th workouts, there was a significant correlation with calcaneal ΔBMC ($r = -0.48$), but only a trend ($r = -0.45$) with ΔBMD as the criterion. No other variables correlated with significant amounts of calcaneal ΔBMC and ΔBMD variance. Negative correlations infer shorter dwell times evoked greater gains. The gravity-independent device warrants continued inquiry to treat and abate calcaneal losses.

1. Introduction

Osteogenesis, whether through diet, drugs or exercise, is typically a slow arduous effort that, at best, yields small improvements over time. Even if the aforementioned treatments are applied concurrently bone growth is, at best, modest [1]. Furthermore treatments to enhance bone mineral content and density (BMC, BMD) must be used for months or even years to derive benefits [1,2]. Regarding exercise, the nature of bone strains imparted is crucial to subsequent changes. The nature of strains relate to their magnitude, rate and frequency. Magnitude is the absolute bone deformation from the exertion of force [3]. Rate refers to the change in strain magnitude expressed as a function of time (Δ force/Δ time). Frequency is a temporal measure of how often strains are applied. It is important that exercise to induce osteogenesis, or a mitigation of losses in disuse models, impart a sufficient combination of strain magnitudes, rates and frequencies.

Exercise protocols and hardware to improve bone health often lack one or more strain-related feature. For instance resistance exercise usually imparts high strain magnitudes, but due to the loads imposed, produce low strain frequencies. In contrast, aerobic exercise and platform vibration protocols have high strain frequencies but low strain magnitudes. Thus while each may evoke modest bone accretion over time, their efficacy is abated since each lacks at least one strain-related feature, which causes some to question exercise's ability to evoke osteogenesis [4]. Research sought to correlate aerobic activity to bone mass, but results were inconsistent [5]. In contrast, some implied bone responds better to non-traditional and/or non-steady state mechanical loading to induce site-specific osteogenesis [6–9]. To further enhance osteogenesis, some believe activities must routinely elicit high strains for short durations to specific bone sites [10–12]. BMD differences

Abbreviations: BMC, bone mineral content; BMD, bone mineral density; Δ, delta; DT, dwell times; I, impulse; IET, inertial exercise trainer; J, joules; N, newtons; $N \cdot s^{-1}$, newtons per second; PA, peak acceleration; PF, peak force; SEE, series elastic element

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among athletes from various sports support this claim [13,14]. Short durations are preferred since skeletal loading stimuli saturates bone after only a few cycles [10,11].

Unlike many studies, a recent chronic training intervention done on high-speed resistive exercise hardware evoked a large osteogenic response to the trained leg's calcaneus [15]. Subjects did 30 left leg workouts on an Inertial Exercise Trainer (IET; Impulse Training Systems, Newnan GA) comprised of three exercises, while their right leg was untreated. They averaged 70 days to finish the workouts, or an average training frequency of 2.3 days, as they refrained from all other structured exercise. Before and after the intervention subjects underwent a series of musculoskeletal tests to both legs, and blood draws. In addition to significant knee and ankle extensor strength gains to the trained leg, that same leg saw significant calcaneal BMC (+29%) and BMD (+33%) gains, while right legs saw non-significant changes. Blood data supported the osteogenic effect, as a significant drop in a bone resorption marker occurred after the 30 workout intervention [15]. Calcaneal osteogenesis was not attributed to muscle mass changes [15].

With an average peak force of 900 N for one of the study's exercises, and Δ force/Δ time average values which approached 2250 $N \cdot s^{-1}$, as well as 2.0–2.5 repetitions per second over one-minute sets, the IET concurrently imparted high strain magnitudes, rates and frequencies [15]. Such a scenario does not occur for typical exercise protocols or hardware. Over the 70-day period subjects provided three 3-day food logs, yet analysis showed non-significant changes to Ca^{+2}, protein and kilocalorie intakes. Thus left leg calcaneal gains were attributed to IET workouts [15]. Our study purpose examines performance variables from the aforementioned project's workout data to identify correlates to left leg calcaneal gains [15]. We hypothesize one or more variables will correlate significantly to the aforementioned project's calcaneal BMC and BMD gains.

2. Methods and materials

2.1. Subjects

Before data collection, the chronic IET training project received human subjects approval from The University of Louisville's Institutional Review Board, which operates in accordance with The Code of Ethics of the World Medical Association. Subjects (2 men, 11 women) gave informed written consent before their participation. All were in good health and free of the following: diabetes, asthma, hypertension, tachycardia, ischemia, arrhythmias, hyperthyroidism and convulsive disorders. Females of childbearing age used birth control which, as shown by a recent meta-analysis, had an indeterminate impact on bone health [16]. They were moderately fit (mean ± sem; age 29.4 ± 3.3 years, men 43 ± 21 years, women 28 ± 3.8 years; body fat % 26.9 ± 0.02, men 18.9 ± 3.9, women 28.3 ± 1.5; mass 69.2 ± 2.7 kg, men 79.1 ± 9.6 kg, women 67.4 ± 3.1 kg) but none had ever used the IET. Thus before the start their 30 workouts, subjects did two familiarization sessions to become accustomed to the IET's operation. Sessions occurred 3–7 days before their first workout. Subjects practiced repetitions at a submaximal level of effort. Sessions were supervised by the principal investigator, who instructed subjects on proper technique.

2.2. IET design and operation

The IET is equipped with a weight carriage mounted on four stainless steel wheels that traverse a polyurethane-coated track to permit movement against very little frictional resistance. A high-strength low-stretch polymer cord is affixed to the carriage's underside, whereby 890 N of force lengthens the cord < 2.8 mm [17]. The cord is interwoven among pulleys to which, at its end, handles may be attached to perform various exercises. Given the IET's design, low forces

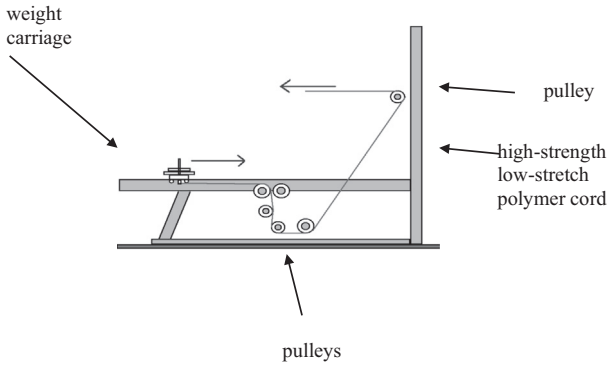

Fig. 1. Side view illustration of the IET.

(~0.45 N) elicit carriage motion [17]. The carriage moves parallel to, but never against, Earth's gravitational pull as repetitions are performed [17,18]. Thus with modifications to meet in-flight hardware specifications, the IET's operation and design may potentially abate musculoskeletal losses incurred with long-term manned space travel. An IET illustration appears in Fig. 1.

To start carriage movement, repetitions require concentric muscle force application. To finish a repetition and continue the exercise set, subjects perform a rapid eccentric action to decelerate the carriage and initiate its movement in the opposite direction. The next repetition begins immediately. With the high-strength low-stretch cord, subjects generate and utilize momentum over succesive repetitions. To quantify performance, the IET is equipped with a load cell (TLL-2 K; Transducer Techniques, Temecula CA) attached to a pulley to measure force. A linear transducer (BTL6-A/C/E/G500-M 1630-PF-S115; Balluf Inc., Florence KY) affixed exactly midway along the track's inferior border measured carriage displacement produced by forces.

Force and displacement data were received by the DI-158 U signal conditioners (DATAQ Instruments, Akron OH) and measured by a analog data acquisition card at 4000 Hz on a computer interfaced with the IET. Force vs. time measurements occurred simultaneously, while the linear transducer quantified the time required for the carriage to pass over the track's midway point. Our instrumentation procedures allowed the capture and display of exercise repetition waveforms in real time. With multiple test-retest measures to examine exercise data from prior IET studies, and instrumentation methods as described herein, data reproducibility exceeded levels deemed acceptable for high-speed repetitions done across consecutive workouts [18].

2.3. IET workouts

Subject's 30 workouts entailed the same protocol. Each began with a bilateral five-minute warm-up on a cycle ergometer (Ergotest, Stockholm Sweden) against a one kilopond load at a self-selected velocity. Subjects then did three IET exercises in the following order: standing knee extension, standing hip extension and seated calf press. Per exercise, they did three 60-s sets separated by 90-s rests. They were told to perform repetitions as rapidly as possible with good form and maximal effort. Rapid changes in direction of the carriage's movement produced an impact force. Waveforms revealed the impact produced the peak force per repetition that corresponded to its strain magnitude. Force changes per unit time, as repetitions proceeded from baseline to peak values (Δ force/Δ time), represent its strain rate. Low-friction IET components enabled performance of 2.0–2.5 repetitions per second over one-minute sets for each exercise. Thus repetitions concurrently imparted high strain magnitudes, rates and frequencies.

To identify performance variables as correlates to the calcaneal BMC and BMD variance produced by the IET intervention [15], we examined workout data for the unilateral hip extension and seated calf press exercises. We chose those exercises from the three performed

Fig. 2. Unilateral hip extension exercise as subject's left leg approaches full extension at the hip and knee joints.

since, in the case of the unilateral hip extension, with concurrent hip and knee extension at the completion of the concentric phase of repetitions (Fig. 2) a large axial load is imparted to the left leg, which positively impacts bone remodeling [19]. In addition that exercise produced among the highest peak force values. We examined seated calf press data due to the potential mechanical loading stimuli it imparts to the calcaneus, as the left leg's ankle serves as the fulcrum for this exercise.

A representative IET repetition waveform appears in Fig. 3. Assessment of unilateral hip extension peak force data revealed values, on average, rose from the first to the 12th workout, and thereafter plateaued. Examination of seated calf press peak force data saw values rose steadily, on average, from the first to the 24th workout, and thereafter plateaued. Since musculoskeletal changes, as well as the degree of adaptation, to training interventions are based in part on subject's initial physical capabilities, we calculated delta (Δ) values for our performance variables to chart their relative degree of improvement over time. Δ values were calculated from repetitions that produced the peak force for the first and 12th workouts for the unilateral hip extension exercise, and for the first and 24th workouts for the seated calf press.

Per exercise we examined four variables as predictors of our criterion measure's variance; each was derived from the repetition that elicited the peak force for the aforementioned workouts. Delta peak force (ΔPF) was included as a predictor variable. Since force is the product of mass and acceleration, delta peak acceleration (ΔPA) also served as a predictor variable. We examined delta impulse (ΔI) since impulses represent a ratio of the change in force relative to the change in time. Finally since carriage acceleration directly impacts repetition rate, we calculated delta dwell times (ΔDT) as the elapsed time from the end of a repetition's eccentric phase and the start of the subsequent concentric phase. DT is characterized by force exertion that leads to eventual muscle shortening, but has yet to evoke visible changes in carriage direction. Each variable was examined as a correlate to

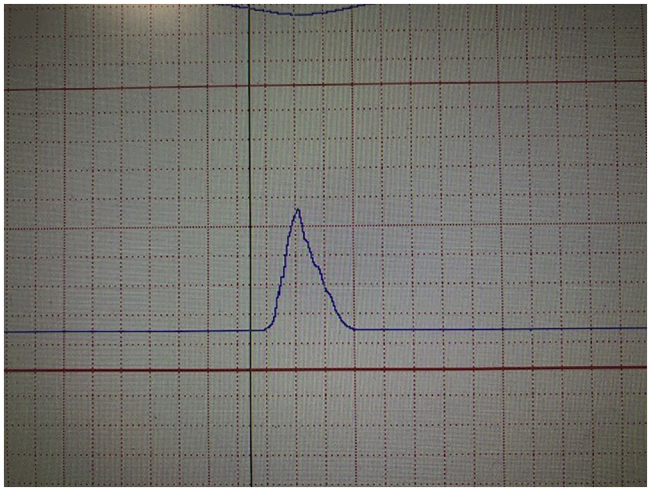

Fig. 3. Repetition waveform that produced a workout's PF value. Force is plotted as a function of time. PF is its highest waveform point. PA was derived from the $f = ma$ formula, whereby f and m were known values. I is the Δ force/Δ time ratio, measured as differences from the repetition's baseline and peak values. The Δ force/Δ time ratio also denotes it's bone strain rate. DT equals the elapsed time from the repetition's end to the start of the subsequent repetition.

calcaneal ΔBMC and ΔBMD values from the IET intervention [15].

2.4. DEXA scans

Subjects underwent DEXA scans on both legs at 4 ± 2.1 days before, and 7 ± 2.0 days after the intervention. A densitometer (Hologic Discovery W; Marlborough, MA), operated by a certified radiologist, carefully quantified calcaneal BMC and BMD. DEXA scans exhibit higher precision than quantitative ultrasound and serve as the gold standard for bone morphology measurements [20]. The procedures employed differed from some reported in the literature, but were consistent over time to enable intra-subject comparisons with the same methods. For our scans, subjects were positioned to examine the calcaneus' medial surface as they lay supine. Per subject, positions were held constant across pre- and post-intervention scans. They were positioned with full external rotation at both hips and 15° of flexion at both knees. The densitometer's forearm software performed the calcaneal scans. Global regional of interest software option was used, followed by adjustment of the Toolbox's line mode in accordance with the scanned image. The computer's mouse was toggeled to draw lines around the calcaneus. Calcaneal ΔBMC and ΔBMD values each served as the criterion variables in the current study's statistical analyses.

2.5. Statistical analyses

Δ values, for both criterion variables, were calculated as post intervention - pre intervention scores. Δ scores from the predictor variables equaled the difference between the first and 12th workout values for the hip extension exercise, and between the first and 24th workout values for the seated calf press exercise. Δ score advantages include they are 1): easy to compute and interpret, 2): based on expected values and not dependent on sample sizes under investigation [21]. Yet their main limitation is the Δ equivalency assumption, which claims the difficulty in expected increases is equal across all performance variables [22]. Pearson coefficients were used to identify the exercise performance variables that were the best predictors of calcaneal ΔBMC and ΔBMD variance [15]. We used ΔPF, ΔPA, ΔI, and ΔDT as predictor variables. $\alpha = 0.05$ denoted significance per analysis. For correlations that reached significance, prediction equations were derived. Finally, to assess collinearity among our predictor variables, multiple bi-variate correlation analyses were run on the four independent variables

Table 1
Pearson product moment correlation coefficient results.

Predictor: unilateral hip extension exercise	Criterion	r	p
ΔPF	ΔBMC	0.24	0.21
ΔPF	ΔBMD	0.23	0.22
ΔPA	ΔBMC	0.08	0.40
ΔPA	ΔBMD	0.11	0.36
ΔI	ΔBMC	−0.34	0.13
ΔI	ΔBMD	−0.34	0.13
ΔDT	ΔBMC	−0.64	0.009[a]
ΔDT	ΔBMD	−0.63	0.01[b]

Predictor: seated calf press exercise	Criterion	r	p
ΔPF	ΔBMC	0.12	0.35
ΔPF	ΔBMD	0.13	0.34
ΔPA	ΔBMC	−0.105	0.37
ΔPA	ΔBMD	−0.11	0.36
ΔI	ΔBMC	0.25	0.20
ΔI	ΔBMD	0.23	0.22
ΔDT	ΔBMC	−0.48	0.048[c]
ΔDT	ΔBMD	−0.45	0.06

[a] Δ BMC′ = 13.281526 + (−0.484191)(ΔDT hip extension exercise).
[b] Δ BMD′ = 0.5684 + (−0.020594)(ΔDT hip extension exercise).
[c] Δ BMC′ = 0.56607 + (−0.100985)(ΔDT seated calf press exercise).

obtained from the two exercises.

3. Results

Data for our criterion and predictor variables were normally distributed. Table 1 shows our Pearson coefficient results. Only ΔDT correlated with significant amounts of our criterion measure's variance. Each ΔDT correlation was negative, meaning shorter dwell times generally led to greater calcaneal ΔBMC and ΔBMD values. With ΔDT values derived from the first and 12th hip extension workouts, there was a significant correlation with calcaneal ΔBMC ($r = -0.64$) and calcaneal ΔBMD ($r = -0.63$). With ΔDT values derived from the first and 24th calf press workouts, there was a significant correlation with calcaneal ΔBMC ($r = -0.48$), but only a trend ($r = -0.45$; $p = 0.06$) towards significance with calcaneal ΔBMD as the criterion. Varying degrees of collinearity were present between ΔDT and the other performance variables. For the seated calf press exercise, r values with ΔDT were − 0.62 (ΔI), 0.32 (ΔPA) and − 0.29 (ΔPF). For the standing hip extension exercise, r values with ΔDT were − 0.12 (ΔI), −0.10 (ΔPA) and − 0.37 (ΔPF). Yet statistical significance was not achieved for either collinearity analysis ($p > 0.05$).

Inspection of our hip extension data from the first and 12th workouts show an interesting effect, namely subjects who had DT values < 26 milliseconds produced positive calcaneal ΔBMC and ΔBMD changes. Conversely those with values > 26 milliseconds saw calcaneal ΔBMC and ΔBMD losses. Of interest is that per subject, DT times were consistent across the workouts examined; meaning they were always under, or over, the 26 millisecond threshold for the hip extension exercise without exception. Figs. 4 and 5 illustrate these relationships for DT values derived from the hip extension exercise.

4. Discussion

Bone responds to local strains imparted by bending and compressive forces provided by mechanical loads. Mechanotransduction converts mechanical load stimuli into an osteogenic effect [15]. Forces exerted against mechanical loads increase Ca^{+2} influx into bone, which activates protein kinases that convert to biochemical signals; collectively the signals are termed mechanosomes [23]. These mechanosomes bind to specific sequences on mechanosensitive genes to regulate their expression [23]. Gene expression within osteoblasts and osteoclasts alters their activity to elicit a net osteogenic effect over time. With 30 workouts done at an average rate of every 2.3 days, our protocol conforms to the idea site-specific osteogenesis best occurs from non-traditional and/or non-aerobic mechanical loads that elicit high strains for short durations to the bone sites of interest [6,8–12,15,25]. Given the IET's design and effort put forth by subjects, concurrently high strain magnitudes, rates and frequencies evoked large calcaneal gains and was the mechanism that caused the 30 workout intervention to elicit site-specific osteogenesis.

Markers of bone formation and resorption were also measured before and after the 30 workouts [15]. Results showed resorption declined significantly after the intervention, yet bone formation increases merely trended towards significance [15]. Thus the IET intervention may have heightened gene expression in osteoclasts that caused a significant decline in bone resorption after 30 workouts [15,23]. In contrast to the IET intervention, stretching in vitro osteoclast cultures led to increased enzymatic activity indicative of heightened resorption [24]. Such results help affirm our assertion, that to evoke osteogenesis, mechanical stimuli must include concurrently high strain magnitudes, rates and frequencies. When this was achieved with IET workouts it coincided with a significant suppression of bone resorption [15]. However such changes do not assure similar bone adaptations to other skeletal sites. Bone changes that vary in magnitude across skeletal regions for a given training program support the idea exercise-induced osteogenesis is site-specific, and different IET protocols may each evoke unique bone adaptations [6,8–12,15,25]. In contrast, prior protocols and hardware that sought to evoke osteogenesis often lacked one or more strain-related feature and only saw modest bone accretion [1–3,13–15,26–35].

While strength training preserves bone, it is a difficult means by which to do so, as years of exercise provides, at best, only modest BMD gains [1–3]. For instance chronic (3–48 months) strength training with heavy (70–90% 1RM) loads 2–5 days per week yielded small (+1–3%) BMC and BMD gains [26–28]. A recent review, which entailed a meta-analysis from 24 trials, with 6–36 month strength training interventions done three times weekly, supports this claim [1]. Another meta-analysis showed only high-intensity resistive exercise was able to preserve lumbar BMD [2]. High-intensity strength training imparts strain magnitudes that may exceed osteogenic thresholds but unfortunately, since repetitions occur slowly, low strain rates and frequencies limit the magnitude of BMD gains even for long-term exericse interventions [3,26–28].

Activities that did not impart sufficient strain magnitudes also limited gains [29–33]. For instance little benefit occurs from race walking, despite high training volumes and long exercise histories of the sport's elites, which was attributed to weak ground reaction forces and resultant low strain magnitudes [34]. Ground reaction forces for race walking are roughly 1.5 times bodymass, which is akin to normal walking but less than running and sprinting (2.5 and 4.5 times bodymass, respectively) [7,19]. Like race walking, chronic whole body vibration or high-speed activity also led to modest changes [29–33]. Whole body vibration's impact on BMD was unclear and deemed contigent upon multiple factors [30,32]. Chronic impact loading from high-speed activity done against light resistance only yielded small (+1–2%) but significant BMD gains [31]. Since PF or I values were not reported, their BMD changes were likely the result of low strain magnitudes [29,33,35]. Similar changes occur to swimmers, an activity known for low strain magnitudes and little high-impact loading [13,14]. Yet given the IET's design and recent study's exercise protocol, site-specific osteogenesis occurred to the trained leg's calcaneus and was the source of a two-way interaction [15]. High PF and I values suggest despite its light (4.4 kg) load, calcaneal osteogenesis occurred [3,15,31]. The IET is predicated on consecutive high-speed repetitions done rapidly. Other studies also assessed high-speed and/or high-impact exercise impact on bone.

A comparison of 70-day interventions, whereby subjects did leg presses on free-weight or flywheel-based hardware twice weekly with

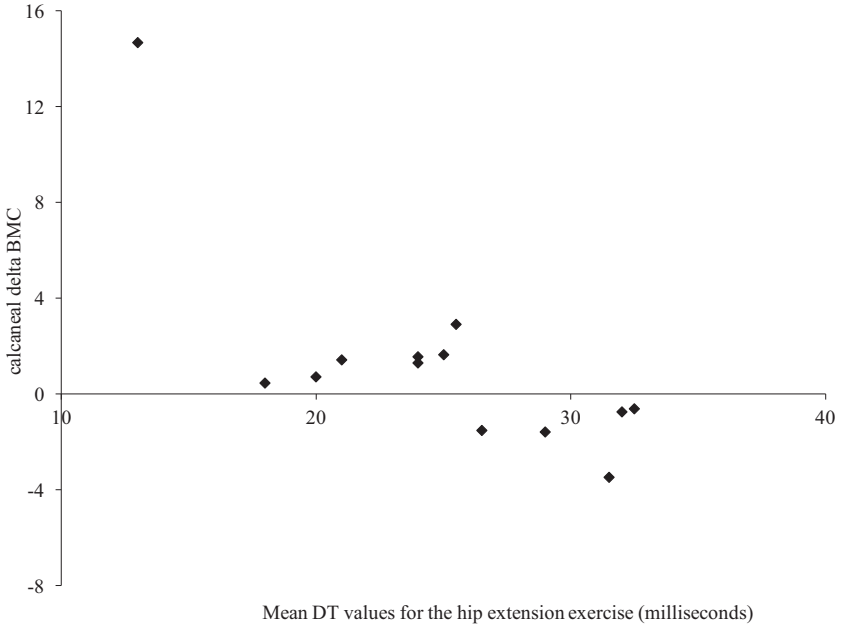

Fig. 4. Calcaneal ΔBMC changes plotted as a function of DT values from the first and 12th workouts for the hip extension exercise.

no crossover, revealed each group had similar improvements except those for BMD [36]. Only free-weight subjects saw BMD gains, which was attributed to their faster repetition speeds [36]. Women continuously wore accelerometers for 12 months as they did impact exercises for 60 min three times weekly and averaged Ca^{+2} intakes of 1000–1100 mg· day^{-1} [31]. Results showed the total impact number was associated with calcaneal accretion [31]. There was also a relationship between the number of impacts achieved with high accelerations and calcaneal accretion, which supports the idea strain rates are more important to osteogenesis than strain magnitudes [31,37]. High-impact training for 12–18 months usually evoke 1–4% BMD gains to weight-bearing skeletal sites in women, with higher gains in younger subjects [33,38–40]. In addition to higher strain magnitudes, rates and frequencies, the IET may be superior at site-specific osteogenesis than other exercise modes since it enables more high-speed and high-impact repetitions. Yet it is important to note, when the IET study's BMC and BMD results [15] are compared to those done previously, to consider the bones examined with each study. Changes induced by exercise or vibration vary in magnitude across skeletal regions for a given intervention, which conforms to the idea osteogenesis is indeed site-specific.

Our hypothesis was affirmed due to the significant amounts of criterion variance that correlated with ΔDT values. This initially appears to be a curious outcome since the IET imparts high bone strain magnitudes, rates and frequencies, which are not unlike our ΔPF, ΔPI and ΔPA variables respectively. The reason ΔDT, and not other variables, correlated with significant amounts of ΔBMC and ΔBMD variance is likely due to the IET's design. Unlike most high-speed exercise, the IET permits high numbers of repetitions to occur rapidly over 60-s sets

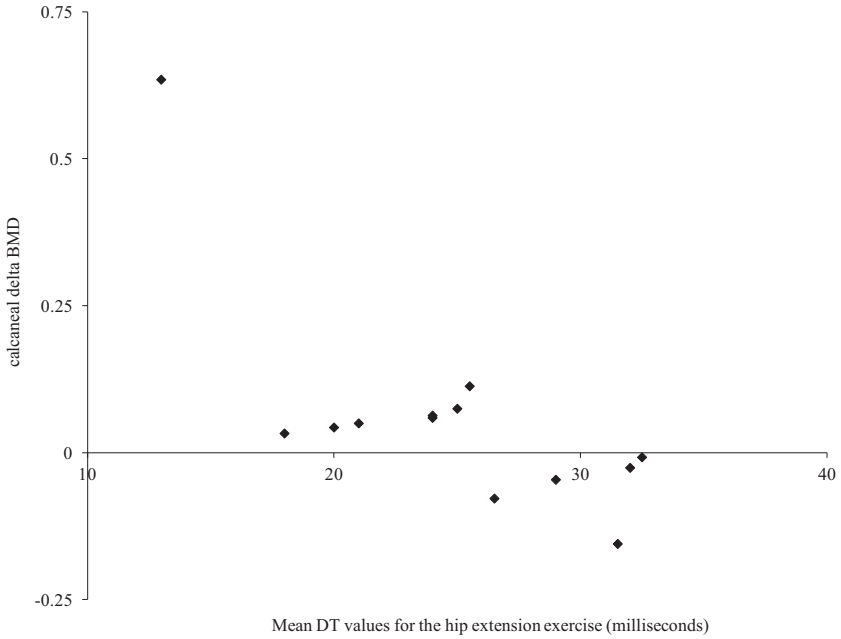

Fig. 5. Calcaneal ΔBMD changes plotted as a function of DT values from the first and 12th workouts for the hip extension exercise.

[18,44]. To achieve this, users must employ momentum over successive IET repetitions; research suggests those sets entail considerable momentum and series elastic element (SEE) utilization which in turn evoke faster movement rates that may reduce DT values with continued training [18,44]. This may explain why ΔDT correlated with more ΔBMC and ΔBMD variance than other predictor variables we examined. Prior research saw SEE utlization's impact on performance, particularly for activities with repetitive high-speed movement [35,36,41–44].

A paradox from prior studies in which high work volumes occurred with modest net energy cost increases, was attributed to SEE involvement during workouts [41–44]. Plantar flexor exercise done on flywheel-based hardware, which sees slower repetition rates than those for the IET, limits SEE involvement and its impact on performance [35]. Yet SEE involvement during seated leg presses on flywheel-based hardware was cited as a reason workouts that also included eccentric actions elicited an additional 3600 J of work with no added net energy cost versus workouts comprised solely of concentric actions [41,42]. However for the seated calf press exercise done on flywheel-based hardware, heightened SEE involvement of the plantar flexors over successive repetitions was cited as a cause for significant declines in integrated EMG values [43]. Results imply the impact of SEE utilization is influenced by the muscle groups examined, rates at which repetitions occur, and the type of exercise hardware employed [35,36,41–44].

The IET does not use gravitational resistance to impart mechanical loads or strains. Thus with modifications to meet in-flight hardware specifications, it may potentially serve as exercise hardware aboard manned space flights. Given the study results from which our data were obtained, whereby IET workouts evoked large calcaneal BMC (+29%) and BMD (+33%) increases over time from reduced bone resorption, this hardware holds much promise [15]. The calcaneus is among the bones that incur the greatest losses from space flight, an environment which sees heightened bone resorption [45]. Prior research confirms the challenges of in-flight exercise hardware to abate bone losses [45]. Such hardware does not impart strain magnitudes, rates and frequencies, or offer high-speed and high-impact repetitions, like the IET.

As women underwent 60 days of bed rest they concurrently received an exercise (flywheel-based ergometry and supine treadmill running), nutrition (high protein diet with 0.6 g/kg of added leucine) or control treatment no crossover. While lower body muscle and strength losses were reduced with exercise, that treatment did not abate unloading-induced bone losses and that further hardware development was warranted [46]. Other studies also saw flywheel-based resistive exercise did not maintain calf muscle force or prevent bone losses with long-term bed rest [47,48]. A combined resistive exercise-vibration treatment also failed to prevent calf muscle atrophy during a 56-day bed rest [49]. Given the aforementioned challenges of exercise countermeasures administered during bed rest to abate bone losses, the IET warrants continued inquiry as a modality to abate musculoskeletal losses seen with simulated and actual space flight.

5. Conclusions

Before concluding it is important to acknowledge our study limitations, which include a small sample and multiple Pearson correlations; the latter increases the risk of a type I error. More research is needed to identify why and how this novel hardware imparted such a unique bone strain stimulus, as well as continued inquiry into ΔDT as a correlate to repetitive high-speed exercise repetitions [15]. In particular emphasis should be directed at the 26 millisecond DT value cited in our study, and its examination as a threshold to calcaneal accretion with IET workouts. In addition the IET intervention described in this paper may prove efficacious in the treatment of other bone loss (osteoporosis, osteopenia, geriatrics) conditions. While the IET subjects were healthy [15], project results give hope to those afflicted with the aforementioned conditions. More research is needed on the efficacy of this intervention to abate bone loss in other disuse models.

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CRediT authorship contribution statement

Steve Davison: Conceptualization, Visualization. **Ling Chen:** Data Curation, Investigation. **Dane Gray:** Investigation, Data Curation. **Bailey McEnroe:** Investigation, Data Curation. **Ian O'Brien:** Investigation, Data Curation. **Amy Kozerski:** Investigation, Data Curation. **John Caruso:** Formal analysis; Funding acquisition; Investigation; Project administration; Supervision; Writing-original draft, Writing-review and editing.

Declaration of competing interest

The authors have no competing interests to declare.

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